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Circular Letters:

Khellin in the Treatment of Angina Pectoris: Khellin is a pure crystalline derivative of Ammi visnaga, a plant that grows wild in the eastern Mediterranean countries, and that is known in Arabic as "khella." The medicinal properties of this plant have apparently been known since ancient times, and a decoction of its seeds has been used by the native populations for many centuries as an antispasmodic for the treatment of renal colic. The first recorded pharmacological study of Ammi visnaga is that of Mustapha, who in 1879 isolated the chief active principle, khellin, in impure form.

Chemically, khellin is a dimethoxy-methyl-furano-chromone with the formula $C_{14}H_{12}O_5$. The findings of Samaan, who suggested the name "visammin" for khellin, indicate that it relaxes visceral smooth muscle by a direct effect on the muscle fiber; Anrep and others have confirmed and extended these observations, pointing out that khellin has an exceptionally potent and prolonged coronary vasodilator effect. Absorption of khellin is rapid, a maximum blood concentration being reached within 30 to 60 minutes after oral administration, and within 5 to 10 minutes after intramuscular injection. It is distributed almost uniformly through all body tissues, and its destruction and excretion proceed so slowly that repeated doses have a cumulative effect. Systemic blood pressure is not altered by therapeutic concentrations of khellin, apparently because the systemic arteries are much less susceptible to its action than are the coronary arteries. No harmful effects on the myocardium, kidney or other organs have been observed, nor has development of tolerance to the drug been noted even after prolonged administration.

Anrep and co-workers have recently reported their observations on the treatment of angina pectoris with khellin. Of 250 patients treated, 225 (90 percent) were considered to be improved: 140 (56 percent) markedly and 85 (34 percent) moderately.

The present study was designed to evaluate therapy in angina pectoris with khellin by controlled objective and subjective methods. Patients with well established angina pectoris were selected from the cardiac clinic of the Boston City Hospital. Preliminary studies on each patient included a medical history, physical examination, blood counts, urinalysis, Hinton test, electrocardiogram, x-ray examination of the heart and, in some cases, cardiac fluoroscopy. Since many of the patients had been followed in the clinic for months or years and had been treated with a variety of medications, some knowledge of their condition and response to therapy was available at the outset. In addition, the severity of the disease was estimated in each patient during a control period of observation by noting the frequency of anginal attacks and the number of nitroglycerin tablets required, and by repeated measurements of exercise tolerance, using the two-step test under standard conditions, essentially as described by Riseman and Stern. Exercise was continued at a comfortable, constant rate until pain became sufficiently well developed to force the patient to stop. After a consistent base line had been established,

therapy was begun and the aforementioned observations were repeated at intervals of 4 to 14 days. Resting electrocardiograms were taken at least once during the period of therapy in most patients, and in 9 cases comparison of the electrocardiographic changes induced by standard exercise before and during treatment was made. Placebos, identical in physical characteristics with khellin, were given either at the outset or after a period of khellin therapy, or both. Khellin was given in the form of sugar-coated tablets containing the equivalent of 40 mg. of the crystalline substance; these were taken orally an average of 4 times daily, after meals and before retiring.

Carefully controlled observations were made on 32 patients over periods ranging from 3 to 10-1/2 months. There were 26 men and 6 women, ranging in age from 49 to 81 years; 2 patients were Negroes and the others white. In addition to coronary-artery disease, hypertension was present in 21 patients, aortic stenosis and insufficiency in 2, mitral stenosis in 1 and diabetes mellitus in 2. The Hinton test was negative in all patients. Thirteen patients had a definite history of one or more myocardial infarctions, and 3 additional patients showed electrocardiographic evidence of old infarctions.

The degree of improvement was classified as marked when anginal pains became infrequent and mild, and when the exercise tolerance either doubled or was apparently prevented from doubling by fatigue, dyspnea or intermittent claudication rather than by anginal pain. Patients were considered moderately improved when nitroglycerin requirements were at least halved (reflecting a corresponding decrease in pains) and exercise tolerance was increased at least one-third unless limited by the nonanginal factors noted. Definite subjectively and objectively measurable improvement of lesser degree was classified as slight.

Of the 32 patients, 26 experienced a decrease in frequency and severity of anginal pains, a drop in nitroglycerin requirements and an increase in exercise tolerance. This improvement was considered marked in 11 patients, moderate in 11 and slight in 4; the remaining 6 showed no improvement. Five additional patients, also treated with khellin, were excluded from this group, either because they were unable to perform the exercise-tolerance test or because they could not be studied for a sufficient period of time. These patients, afflicted with severe and at times intractable angina, all experienced moderate or marked reduction in frequency and severity of pains and in nitroglycerin requirements.

Although patients were observed for periods varying from 3 to 10-1/2 months, the duration of khellin therapy ranged from 7 weeks to 9 months; the average duration of treatment for the 32 patients exceeded 4 months. Effective daily khellin dosage ranged from 120 to 240 mg.,with an average of 160 mg. Of the 26 patients who improved with khellin therapy, the dose required for optimum benefit was 120 mg. in 7 patients, 160 mg. in 13, 200 mg. in 3 and 240 mg. in 3. Of the 6 patients who did not improve, 1 could tolerate only 80 mg., a second 120 mg. and a third 200 mg.; 2 were not given doses exceeding 160 mg., and one was not

given a dose exceeding 200 mg. In all but the latter 3 patients, the daily dose was gradually raised by 40 mg. increments to a level which effected either satisfactory improvement or a toxic reaction. Frequently, the dose required for maintenance of improvement was less than that needed to initiate it, although no attempt was made to determine the minimum effective maintenance dose in each case. Improvement began within 1 or 2 weeks after an effective dose was given. No correlation was noted between the severity of angina and the dose required.

Toxic reactions to therapeutic doses of khellin (gastric irritation and insomnia) were generally not severe. Nausea and vomiting limited the daily dose to 80 mg. in one patient and 120 mg. in another; khellin therapy could not be evaluated in a 3d patient because of inability to tolerate the initial daily dose of 120 mg. Transient, mild nausea and vomiting occurred in 3 patients during the first few days of treatment but thereafter subsided and did not recur in spite of continuation of the same dose. Mild anorexia was noted in two cases but was not sufficiently troublesome to interfere with treatment. One patient complained of vague epigastric discomfort, while another experienced troublesome insomnia unless his maintenance dose was taken early in the day. Six additional patients, who had improved with small or moderate doses, noted similar untoward reactions when doses were administered in an effort to induce further improvement. Miscellaneous complaints, including mild dizziness and constipation, at first thought to be related to khellin therapy, were subsequently found to occur in the same patients while receiving a placebo or no treatment at all. In order to lessen gastric irritation, khellin was given in divided doses of 40 to 80 mg. following meals; an additional dose taken at bedtime by several patients was well tolerated with the single exception noted previously. No significant alterations in blood pressure were observed during the period of khellin treatment. The only death in the series, due to acute myocardial infarction, was that of a patient while he was receiving khellin. There were no adverse reactions to the exercise tolerance test.

The resting electrocardiogram was not altered by khellin treatment. In 9 patients electrocardiographic changes induced by standard exercise before and during khellin therapy were compared; khellin therapy had no effect on the electrocardiographic changes in 5 patients, diminished them in 2 and eliminated them in two others.

Comment. The difficulty of evaluating drug therapy in angina pectoris is well known, and results largely from irregular and unpredictable variations in the severity of the disease. Spontaneous remissions often occur; these may be attributed to decreased activity or emotional stress, warm weather, avoidance of overeating and other precipitating causes, improvement in collateral circulation and, probably, other obscure factors. The problem is further complicated by the psychologic effects of new medication and sympathetic medical attention.

The authors' knowledge of the previous condition and response to therapy of many patients, supplemented by the information obtained during the control period

of observation, provided a valuable basis for comparison. The general level of physical activity of each patient remained approximately constant throughout the period of study, except in those cases in which an increase was associated with beneficial effects of treatment. The time of treatment was such that in many patients improvement occurred during the cold winter months, when exacerbation of symptoms was expected on the basis of previous experience. The rapid action of khellin, by making evaluation of its effects possible within a short time, minimized the opportunity for improvement due to extraneous factors. The use of placebos, particularly when given at the outset, permitted estimation of the influence of psychic and other factors unrelated to khellin therapy. Recording of the exact number of anginal pains experienced and nitroglycerin tablets required with a known level of activity served not only as an index of the patient's condition, but also as a check on his subjective estimate of his own condition. The use of standardized exercise tolerance tests during all phases of observation, particularly when combined with recording of electrocardiographic changes, provided an objective means of assessing khellin therapy. Although each of these methods of evaluation, including the so-called objective ones, may be subject to certain inherent shortcomings and inaccuracies, the closely correlated results obtained by essentially independent methods, together with the striking degree of improvement frequently observed, appears to constitute reliable evidence of the efficacy of khellin therapy.

It is not surprising that nearly one third of the patients showed little or no improvement in view of the advanced coronary-artery disease present in the group; the latter is substantiated by the high incidence of previous myocardial infarctions. Other workers have stated that approximately 30 to 40 percent of patients with angina pectoris do not respond to drug therapy, presumably because their collateral circulation is not capable of increased compensatory dilation. The problem is further complicated in the case of khellin therapy by the fact that some patients are unable to tolerate therapeutic doses. One patient who experienced sustained improvement with khellin therapy, again developed severe angina 2 months after therapy was discontinued. A second course of khellin failed to bring about appreciable improvement, presumably because of progression of the disease during the period of no treatment.

There is no doubt that large doses of khellin, or possibly impurities contained in present preparations, are capable of producing undesirable side effects in many patients. However, most patients can tolerate therapeutic amounts given postprandially in divided doses, and the incidence and severity of toxic reactions may be minimized by the use of small initial doses, with gradual increases until optimum improvement is achieved. In this study, an initial daily dose of 120 mg. for 2 weeks, with increments of 40 mg. at weekly intervals thereafter, was found to be a satisfactory schedule. After improvement has occurred, a smaller maintenance dose may be adequate. Whether the toxic effects are due to impurities or to the khellin itself remains to be determined; the elimination of insomnia in one patient by administration of the daily requirement early in the day suggests the

possibility that this side effect, at least, is due to a rapidly excreted impurity. The high proportion of favorable results, together with the striking degree of improvement frequently observed, has led the authors to the conclusion that khellin, properly used, is a safe and effective drug for the treatment of angina pectoris. (New England J. Med., 1 March '51, H. L. Osher et al.)

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Studies of Radiogallium as a Diagnostic Agent in Bone Tumors: This is a report of the first 18 human subjects in whom radiogallium tracer studies have been made at the U. S. Navy Medical Center, Bethesda, Maryland; all had primary or secondary malignant processes of the bone.

Laboratory studies of the pharmacology and biochemistry of gallium have shown that this element is selectively localized in osteoid tissues and particularly in centers of osteogenesis. The present study was done (a) to develop methods for the localization of $Ga^{72}$ in the human body, by an externally positioned Geiger tube, and (b) to determine the degree of localization of $Ga^{72}$ in patients with neoplastic lesions involving bone. Gallium is a metallic element having many of the chemical properties of aluminum. The radioactive isotope ($Ga^{72}$) is a $\beta$ and $\gamma$ emitter, of energetic spectrum (max. $\beta$ 3.1 mev, $\gamma$ 2.5 mev). This isotope is contained in carrier gallium (0.1 mc. per milligram Ga) and administered as the citrate.

The patients were primarily selected from those with proved malignant lesions, having x-ray evidence of new bone production, or metastatic lesions in bone. Later it was found that patients having localizing bone symptoms but without x-ray confirmation were also suitable for these diagnostic studies.

Radiogallium ($Ga^{72}$) was administered as a citrate complex (300 to 400 $\mu$c.) accompanied by 3.8 to 5.0 mg. carrier gallium, contained in 1 cc. of solution. The $Ga^{72}$ citrate solution was measured in a lead-shielded tuberculin syringe and injected into the rubber tubing of an intravenous infusion drip apparatus. The antecubital vein of the arm was used as the point of administration. The injection was made in one minute. No adverse local or generalized reactions have been observed in any case.

Suitable points on the body of the patient were marked with indelible ink. Posteriorly, these included 12 points, every 5 cm. along the spine and 2 series of points laterally over the pelvis. Anteriorly, points were marked as follows: 2 rows of 6 points, from each groin superiorly to the 2d intercostal space. Two additional points were located on the upper and lower points of the sternum. The Geiger tube was localized over each point at the surface of the body and a 1-minute count recorded. By counterbalancing the jacketed tube, it was possible to maintain the end of the shield gently pressed against the skin surface. No undue discomfort to the patients resulted.

The pattern of counting areas included 40 points. Each series of counts required approximately 1 hour. Counts were made at 3, 10, and 24 hours after the intravenous injection of the tracer dose of $Ga^{72}$ (300 to 400 μc.) With this dose it was possible to obtain counts of 600 to 1,100 per minute at the skin surface of the patient 3 hours after administration of the $Ga^{72}$. The background rate of the tube used is 7 to 9 counts per minute. The addition of counts, taken directly over the xyphoid process at 30 cm. and 90 cm. distances, each count for 3 minutes, was made in the last 5 cases of the series. This would tend to indicate the rate of concentration change in the trunk of the patient and act as a base line for comparison of concentrations within each localized area. The biologic half-life as determined by the method in the human patient is 12 to 13 hours.

A significant aid in determining the areas of localization of gallium in various tissues has been the determination of the relative increase of $Ga^{72}$ during the 3 to 24-hour period after intravenous injection of the gallium citrate. The observed Geiger-Müller count over a certain point at 3 hours after injection is taken as a reference value. The counts over this exact point at 10 hours and 24 hours, when corrected for decay to the 3 hour time ($T_{1/2}$ = 14.3 hr.), will indicate whether there has been an increased deposition of gallium in the structures beneath the counting point.

In many normal tissues the amount of gallium will decrease, as indicated by the foregoing calculations. However, in many areas of bone involvement there is a marked increase in deposition of gallium as indicated by the external counts. This fact has proved most significant in these diagnostic studies.

Intravenous tracer doses of $Ga^{72}$ citrate were selectively concentrated in the osteoid lesions, both osteogenic and osteolytic, in 15 of the 18 cases of primary and secondary bone malignancies. It was found that concentration of $Ga^{72}$ in malignant processes involving bone approaches 20 times that found in the adjacent bone. In some cases, early metastases to bone were identified through tracer amounts of $Ga^{72}$ before changes could be identified by x-rays. (J. Lab. & Clin. Med., February '51, Cdr W. C. Mulry, MC, USN, & Cdr H. C. Dudly, MC, USN)

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Endometriosis, Clinical Aspects and Therapeutic Considerations: Endometriosis presents two distinct characteristics: (1) a foreign invasion of the endometrial cells; and (2) destruction of hemorrhagic extravasations of the menstrual cycle and subsequent formation of blueberry and tarry cysts and adhesions. The resulting pathologic sequelae and symptomatology depend upon the mode of spread of the disease and the response to ovarian hormones. Endometriosis exhibits some of the properties and propensities of new growths and sequelae similar to those of inflammatory affections.

This study comprised 88 operative and histologically proved and 74 clinical cases from a series of 2,000 consecutive private patients with varied gynecological

complaints. The diagnosis of endometriosis was made 162 times, an incidence of 8 percent. This figure seems to coincide generally with the ratios in extensive data collected by others, indicating that endometriosis occurs more often in private than in ward patients. The explanation has been offered that in the so-called upper classes of society marriages are likely to occur late and pregnancies are thus postponed, so that there are many recurring menstrual cycles in which hormonal reactions stimulate the celomic cells to produce Müllerian growths. In this series, 59 of the 88 operative cases and all of the 74 suspected clinical cases were primarily infertility problems.

Approximately 80 percent of the patients with external endometriosis were in the age groups of 26 to 40 years, and approximately 75 percent of those with internal cases were in the age groups of 36 to 45 years. The symptoms in all groups were manifold, the most common being a characteristically progressive dysmenorrhea, menstrual abnormalities, and low abdominal pain. The most frequent physical findings were cul-de-sac tenderness and irregularity, palpably enlarged ovaries, tender adnexa with or without induration, and uterine enlargement almost invariably due to coexisting fibromas.

Prolonged childlessness was frequent in all types. The patients generally gave a history of long use of contraception and this may indicate that endometrial lesions may be caused by deficiency of endocrines which are normally produced during pregnancy. Accordingly, early marriage and frequent child-bearing may be regarded as prophylactic factors. However, endometriosis may develop despite previous pregnancies, and women with no signs of endometriosis may be sterile.

Treatment was preferably expectant and conservative, especially in young women, with a view to preserving ovarian and gestational functions. Surgery was resorted to only when symptoms were uncontrollably progressive. In older women, however, there was no hesitancy about radical procedures.

There appeared to be no significant differences in the number of pregnancies resulting from conservative surgery, palliative therapy or no therapy in women in the same age groups. There was no correlation between prognosis and the amount and location of endometrial lesions, the postoperative symptomatic relief, and subsequent pregnancies.

No definite and fixed rules for individual cases can be derived from group studies. (Am. J. Obst. & Gynec., January '51, S. L. Siegler and J. R. Bisaccio)

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Impacted Fractures of the Neck of the Femur: Somewhat less than 10 percent of fractures of the anatomic neck of the femur are impacted. It is generally

agreed that if impaction is maintained, union will occur. About half the authors of textbooks on fracture recommend nailing; the other half recommend no operative treatment. Because of the impaction, it is the authors' opinion that the treatment demands specific consideration. Once disimpaction occurs, the advantages in treatment of this fracture are lost. The peril of disimpaction is very real and can occur with alarming ease during nailing with a three-flanged nail.

The mechanism of fracture is most commonly that of falling with the body weight on the greater trochanter, thus impacting the fractured ends. A second mechanism is that of wide abduction and deep extension of the hip. Simple rotation of the femur may produce a fracture, but cannot cause impaction. The impaction is usually on the superior aspect of the fracture line and frequently on the posterior surface.

This discussion is based on a study of 50 patients with impacted fractures of the anatomic neck of the femur. The story is different from that of unimpacted fractures. There is frequently a history of weight-bearing on the affected limb for a few steps or even for a few days. The diagnosis of sprained hip is frequently made. The patient is able to lift the extended leg in spite of pain. The limb can be actively rotated. No external rotation deformity is present, and there is no appreciable shortening.

Accurate diagnosis is made only by roentgen examination; therefore, pain about the hip following a fall or other injury demands x-ray study, with anteroposterior and lateral views taken for complete diagnosis. The lateral view is taken through the perineum. The well hip is flexed out of the way. The lateral view will show rotation of the femoral head (if present) and the general alignment of the head with the neck of the femur. The 2 views will help to determine the depth of impaction.

Since only certain impacted fractures are suitable for nonoperative treatment, the classification and description of these fractures is important. The criteria for classification are (1) the degree of impaction and (2) the relation of the femoral head to the femoral neck. Impaction up to 3/4 inch (1.9 cm.) may be observed on the films. Impaction of less than 1/4 inch (0.6 cm.) is not satisfactory for nonoperative treatment.

Pauwels' classification of abduction and adduction fractures is based on the angle formed by a line drawn through the anterior-superior iliac spine and another drawn through the fracture line. If the angle is 30 degrees or less the lesion is called a Pauwels I fracture. A Pauwels II fracture is one with an angle of 30 to 50 degrees, and an angle of 50 to 70 degrees indicates a Pauwels III type of fracture. In fractures of the Pauwels I type the stress is conducive to impaction.

According to the authors' classification, these fractures are of 3 types: Type I are subcapital abducted fractures, soundly impacted and with good

alignment of the femoral head to the femoral neck. These are usually of the Pauwels I type. Type II are cervical impacted fractures, with or without abduction, with good alignment. These may be Pauwels type II or III. Type III are all other impacted fractures of the neck of the femur with malalignment.

The treatment selected in each case depends on the type of fracture. Many orthopedic surgeons prefer internal fixation for all fractures of the femoral neck, but in the authors' opinion internal fixation is often unnecessary. When it is used, the instrument of fixation must absolutely minimize the danger of disimpaction. Over the years, the senior author has twice disimpacted such a fracture while inserting a flanged nail. The nail was easily driven through the neck of the femur, but disimpaction occurred when it engaged the more compact bone of the femoral head. Later Granberry wires were used in a few cases; the wires were drilled into the bone.

The greatest danger is careless handling of the patient, especially during anesthesia. Since 1937 the sandbag pillow splint has been used for Type I fractures, with gratifying results. Heavy traction is to be avoided, because impaction may be lost after relaxation of the muscle spasm. A winged plaster boot or bilateral boots joined by a crossbar may be used to prevent external rotation. Neutral or slight internal rotation must be maintained and adduction prevented. Considerable activity is allowed. A trapeze is placed over the bed. This allows the patient to raise himself for nursing care. A back rest is allowed at all times. The patient is urged to take deep breathing exercises many times daily. Massage is given to the abdomen, groins, thighs and calves several times daily. Muscle-setting exercises for the affected limb are beneficial. Such a program will greatly diminish the incidence of complications. (This treatment should not be called watchful expectancy.) Walking with support is allowed at approximately 6 weeks.

Type II fractures are impacted with or without abduction (valgus). They are usually fractures of the Pauwels I or III type, which involve the neck rather than the subcapital portion of the femur. The shearing stress at the fracture is conducive to disimpaction, especially during the period of absorption at the fracture line. Internal fixation may be chosen for the treatment of this fracture. Reduction is not necessary, and impaction must be maintained; therefore, the authors prefer an internal fixation splint which requires drilling rather than pounding for its insertion. It is true that impaction will not always be lost, especially if the nail is inserted exactly in the center of the head, but perfect insertion of a flanged nail is difficult in an abduction fracture. Loss of impaction occurs frequently enough to warrant particular care.

Type III fractures may be deeply impacted. The alignment of the head to the neck of the femur is not acceptable. Therefore, disimpaction and reduction are required. The surgeon may use whatever type of internal fixation he prefers.

In this series there were 42 women and 8 men. The average age was 62 years, excluding one 33-year-old patient. The fractures were classified as 37 Type I, 4 Type II and 2 Type III. Seven could not be classified because the films had been destroyed or lost. Only 1 of the Type I (valgus) fractures became disimpacted and required internal fixation. One Type II fracture became disimpacted when nailed. (There was another such case, the record of which cannot be found; this case was omitted from the series.) Thirty-five Type I, 2 Type II and 1 Type III fractures united without internal fixation; 5 fractures were treated by internal fixation, with union.

Complications. Two patients, 77 and 78 years old respectively, died of direct complications. One 33-year-old patient continued to have a painful hip and died of cirrhosis of the liver 23 months after injury. Nonunion occurred in 1 hip. In 2 hips, avascular necrosis developed after union. One of these hips, with a fracture of Type I, healed without internal fixation. The other,with a fracture of Type II, became disimpacted on insertion of a Smith-Peterson nail and united; avascular necrosis developed later. This patient had a 5/8 in. (2.8 cm.) impaction. This group is too small to evaluate such complications as avascular necrosis and nonunion.

The senior author was so convinced of the merit of nonoperative management that his own Type I fracture was treated without surgical intervention. (J. Internat. Coll. Surgeons, February '51, G. J. Garceau and H. W. Sigmond)

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Effects of Oxygen, Analeptics, and Artificial Respiration on the Toxicity of Procaine: The introduction into the blood stream of procaine in sufficient amount to cause a sudden high concentration is thought to cause circulatory collapse or "cardiac death," while a gradual increase in blood procaine produces a central stimulation which is followed by depression with eventual respiratory failure. If this be true, the most frequent cause of death from slow intravenous infusions of procaine should be respiratory failure. Such has been reported to be the case, although cardiac and respiratory failure may occur almost simultaneously. Experiments designed to study the effect of anesthesia and the rate of injection on blood levels and toxic reations during intravenous infusions of procaine permitted preliminary observations on the cause of death from such administrations. In 81 out of 83 experiments on dogs, the heart continued to beat for from 30 seconds to 8 minutes after respiratory movements ceased. In the other 2, heart apparently stopped at the same time as respiration. It is of interest that these 2 dogs were anesthetized with ether, which has been shown to sensitize animals to procaine. These observations stimulated the authors to study in more detail the cause of death from slow intravenous infusions of procaine and to evaluate experimentally the therapeutic effectiveness of analeptics, oxygen, and artificial respiration.

Controls. Eleven experiments were run in which the dogs breathed air. Blood pressure and respiratory movements were recorded on a kymograph by means of a mercury manometer and a Manning pneumograph. The condition of the heart was also checked with a stethoscope and respiratory movements by close observation of the animal. Ether was administered to produce light anesthesia for from 30 to 45 minutes before the procaine infusion was started. The procaine hydrochloride was injected as a 1 to 5 percent solution in normal saline by way of the right femoral vein at a constant rate of 2 mg./Kg./min. The infusion of procaine was continued until respiratory movements ceased, at which time it was stopped. The ether was discontinued when the procaine infusion was started and thereafter was administered in the minimal amount necessary to prevent voluntary movements. The times for both respiratory and cardiac failure were noted. At the moment of respiratory failure, blood was obtained from the left femoral vein and its content of procaine and p-aminobenzoic acid determined by a modified Bratton-Marshall method for sulfonamides.

Oxygen. Ten dogs were treated in the same manner as the controls with the exception that they were allowed to breathe 95 percent oxygen at atmospheric pressure. A constant flow of oxygen was employed and rebreathing was not permitted. The oxygen was administered from the start of the procaine injection until respiratory failure, at which time the oxygen was discontinued.

Analeptics. Other groups of dogs received in addition to oxygen, intravenous injection of analeptics as soon as possible after complete cessation of all respiratory movements. The dose of these drugs varied and was given either as a single injection or in divided amounts at 30 second intervals. The total amounts of the drugs given, expressed as mg./Kg. were: nikethamide, 70 to 500; metrazol, 25 to 150; picrotoxin, 1 to 10; and lobeline 0.4 to 0.9.

Artificial respiration. Series A. Three experiments were performed in which oxygen was administered under slight pressure. This procedure was the same as those with the oxygen experiments except that the oxygen was continued after respiratory movements had stopped. Series B. Three experiments were performed as under oxygen with the institution of artificial respiration at respiratory failure. In these experiments, the procaine infusion was not stopped until the blood pressure had fallen almost to zero. Series C. Eight dogs were infused with procaine in the same manner as the controls. After the respiratory movements had stopped, and a blood sample had been taken, the blood pressure was carefully watched until it began to fall rapidly and the heart sounds became weak. At this point artificial respiration was started in an attempt to save the animal.

As a result of these experiments, it was observed that: (1) The primary cause of death from intravenous procaine when used as an adjunct to general anesthesia is hypoxia due to respiratory failure. (2) If hypoxia is great at the

time of respiratory failure, heart failure may occur almost simultaneously. (3) Nikethamide, metrazol, picrotoxin, and lobeline are of no value in respiratory failure resulting from prolonged intravenous infusions of procaine. (4) Oxygen administration and artificial respiration are life saving if instituted promptly. (Proc. Soc. Exper. Biol. & Med., January '51, H. R. Hulpieu and V. V. Cole)

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Nasopharyngeal Malignant Tumor: A nasopharyngeal malignant growth, while not the most frequent, is possibly the most serious growth of the head and neck, and has a reliably estimated 3 percent incidence of tumors in that area. Located in a region designated by Carmody as "the epipharynx, the almost unknown in otolaryngology," the bizarre pattern of initial symptoms diverts attention. Inaccessibility of easy examination and biopsy complicates the problem and symptoms of the primary growth may be so overshadowed by metastases that patients undoubtedly die of widely disseminated malignant changes with the actual site of the causative lesion in the nasopharynx unsuspected.

The author reports a study of 5 cases in personal practice, 10 cases from the private practice of interested colleagues, and 9 cases from institutional practice at the University of Colorado Medical Center from 1940 to 1949 inclusive. Only the cases of true histological malignancy were studied. Two patients in the author's series were 2-1/2 and 3-1/2 years old respectively.

Males are affected more than females in a predominance variously reported at 60 to 90 percent. A racial susceptibility has been noted in Orientals, especially the Chinese, even those American-born. Gardham stated that in Hong Kong 25 percent of all surgical malignant lesions were in the nasopharynx. Wang of Chengtu collected 36 cases in a short period, one-third in patients between the ages of 25 and 35, only 3 of whom were females; 92 percent were carcinoma of some type and extension into the skull involved one or more of all cranial nerves except the 4th and 8th.

Metastases occur almost universally to the cervical glands, in some instances before the primary lesion can be detected. The glands most commonly noted are immediately posterior to the angle of the mandible along the anterior border of the sternocleidomastoid muscle; the posterior cervical chain may also be involved early. Later metastases occur to the liver, lung and osseous system, especially the vertebrae.

The signs and symptoms of this nasopharyngeal malignant process are such that one may be led astray in the early phase of the disease, and there is some variation according to the pathological character of the tumor. Sarcoma produces more evidence of nasal obstruction and bleeding, whereas epithelial tumors are more apt to produce symptoms referable to the cervical glands, aural and cranial nerves. Recognition of signs and symptoms depends on an adequate history and careful examination. Simmons and Ariel found that neck

swelling was the earliest symptom, pain in the side of the face and head and symptoms of cranial nerve involvement were next in frequency. An average of 10.1 months elapsed from the time of the earliest symptoms until diagnosis. Otalgia, stuffiness in the ear, conduction deafness and tinnitus caused by pressure on the pharyngeal orifice of the eustachian tube are common early symptoms. There is an irresistible tendency of the tumor mass to extend upward and to invade the base of the skull, with resultant cranial nerve symptoms. Figi evolved a characteristic symptom complex consisting of deep-seated pain in the frontotemporal region; tinnitus, aural pain, and deafness; neurological signs referable to the 2d, 3d, 5th, 6th, 9th, 10th, and 12th cranial nerves, the commonest being external rectus palsy and a metastatic mass in the neck, which often preceded other symptoms by several months. Thus, the symptoms of this malignant lesion are seldom referable to the local lesion except by inference. The possibility of such a lesion should be kept in mind in any case of unilateral otalgia, tinnitus, deafness, unilateral cervical adenopathy, and signs of cranial nerve disturbances. Biopsy of suspected tissue is imperative for accurate diagnosis and as a means to prognosis and treatment. Specimens may be secured with a biting forceps via the nose with a mirrow in the pharynx as a guide, or tissue may be removed under direct vision by the Yankauer instrument. Repeated trials may be necessary in small early lesions. As an adjunct to but not as a substitute for biopsy, an adaptation of the Papanicolaou technic for locating malignant cells with smears may be used. X-ray may give valuable assistance both as to the character and extent of the tumor and as to the erosion of the bony structure at the base of the skull.

The concensus of studied opinion is that roentgen ray therapy of the primary lesion and cervical metastases with or without cavitary use of radium or radon is the treatment of choice. The 5-year survival rate is quoted as not more than 20 to 25 percent of cases. Lymphosarcoma and lympho-epithelioma yield a better prognosis than the various types of carcinoma. (Arch. Otolaryng., January '51, H. L. Hickey)

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Radiocobalt in Otolaryngology: Radiocobalt is an effective, efficient source of gamma radiation, comparing favorably with radium in this respect. It has the further advantage of producing a monochromatic, homogeneous radiation of high intensity that is accompanied with only a small percentage of relatively weak, unwanted beta radiation. This beta radiation is completely screened when a silver plating to a thickness of 0.08 to 0.16 mm. is used.

The radiocobalt is used in the form of beads which are fabricated before the metal is made radioactive. The metal cobalt is cheap and can be fabricated into any desired shape or form prior to activation, thereby eliminating any industrial hazard of working with a radioactive material. In the human body, the use of radioactive beads has the advantage of a closer approach to a "point source" of radiation.

A Foley catheter with the tip cut off is used for application of the bead because these catheters are available in sizes from 5 to 70 cc. capacity, permitting the selection of one of the proper size for the particular cavity area. Moreover, use of the catheter permits centering of the radiocobalt bead and the assurance that it will remain in place.

Radiocobalt has no particular affinity for body tissues and is rapidly eliminated. It does not, therefore, present the same hazard as radium, should it or its salts in any way accidentally gain entrance to the body fluids.

The relatively short half-life of 5.3 years is the only disadvantage radiocobalt presents when compared with radium as a source of gamma radiation.

The initial local reactions are the same as those obtained after exposure to similar doses of radium. The period of observation thus far is much too short to warrant any evaluation of the results. Present knowledge permits the conclusion that the gamma radiation from radiocobalt is similar to that from radium, and therefore results may be anticipated similar to those obtained with use of radium. If this observation proves to be true, there is no reason why radiocobalt cannot be used in place of the usual radium applicator. The several advantages radiocobalt offers would suggest its use in preference to radium. Owing to the fact that radiocobalt emits gamma rays of high intensity, the same precautionary measures for handling, use and storage that apply to radium must be instituted and followed in order to protect the patient and the personnel. (A.M.A. Arch. Otolaryng., February '51, L. F. Morrison)

In the discussion which followed presentation of this paper, Dr. B. V. A. Low-Beer remarked that radiocobalt has been useful not only in treatment of tumors of the maxillary sinus and nasopharynx, but it has also proved valuable in the treatment of urinary bladder tumors and should constitute an ideal radiation source for treatment of uterine body cancers.

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Atrial Flutter. Methods of Treatment: Even though the mechanism of atrial flutter has been considered by some to be the same as that of atrial tachycardia, its response to therapy is definitely different. There appears to be a general agreement that the circurhythmia should be abolished, preferably by reversion to sinus rhythm, but if that is not possible, by reversion to atrial fibrillation. Although digitalis decreases the ventricular rate in atrial flutter by increasing the degree of atrioventricular block, exercise in digitalized patients with persisting flutter may temporarily decrease the grade of block and thus produce periods of rapid ventricular action. Atrial fibrillation is generally considered preferable to atrial flutter because the ventricular rate in atrial fibrillation is easier to control.

There is no unanimity of opinion regarding the treatment of choice in atrial flutter. Most schemes for reversion employ digitalis preparations or quinidine, singly, in sequence, or in combination. It is probable that the optimum schedule varies with the clinical condition of the patient and the duration of the disorder.

The management of atrial flutter may fail at each point of the desired sequence of events. Following adequate digitalization, the arrhythmia may persist. Other patients may remain in atrial fibrillation permanently after conversion from atrial flutter. Rarely patients may be transformed apparently directly to sinus rhythm. However, in some cases in which there has been direct conversion, the temporary state of atrial fibrillation may well have been missed. Institution of quinidine therapy has been occasionally successful in restoring sinus rhythm if fibrillation persists after digitalis has been withdrawn.

In a recent analysis of atrial flutter occurring 93 times in 82 patients, it seemed desirable to determine the indications and effectiveness of the various therapeutic methods used to terminate the disorder. The patients were seen and treated at the University of Texas School of Medicine in the past 22 years. The cases were divided into transient and established flutter, depending upon whether the duration of the disorder was less or greater than an arbitrarily chosen period of 72 hours. Since the different methods used in various cases were generally well documented, an opportunity was offered for comparison of their efficacy. There were 28 episodes of transient (less than 72 hours' duration) atrial flutter in 24 patients and 55 episodes of established (more than 72 hours' duration) atrial flutter in 48 patients.

Digitalis is the drug of choice in the management of atrial flutter in patients with serious organic heart disease or cardiac decompensation, or where there is specific contraindication to quinidine. It usually acts by instituting atrial fibrillation, which reverts to sinus rhythm on its withdrawal, particularly if quinidine is then given. Even in the refractory cases, or when permanent atrial fibrillation is established, the slow ventricular rate maintained by digitalis provides for adequate cardiac function. Digitalis may also convert the atrial flutter directly to sinus rhythm, but in some of these cases a temporary period of atrial fibrillation may be missed.

With the exception of increased rapidity of digitalization, the pure crystalline oral and intravenous digitalis glycosides showed little advantage over digitalis leaf in this series. However, these preparations were outstanding in certain individual cases and deserve further study.

Oral quinidine sulfate alone proved effective in restoring sinus rhythm in selected patients without cardiac decompensation and without grave organic heart disease, particularly if the atrial flutter was of short duration. It has the disadvantage of being a myocardial depressant and on rare occasions initiates 1:1 conduction with the hazards of a rapid ventricular rate.

In unusually refractory cases, when previous attempts have been unsuccessful in influencing the circurhythmia, intravenous quinidine lactate or gluconate may be justified in the attempt to institute sinoatrial rhythm, but only with frequent blood determinations and under constant, direct electrocardiographic control.

Combinations of quinidine and digitalis concurrently were less effective than either alone or in sequence, but they appear desirable whenever atrial flutter occurs in acute myocardial infarction with cardiac decompensation, and when 1:1 rhythm has once developed with quinidine alone. Maintenance doses of quinidine, potassium or possibly Cedilanid are variously dependable after reversion in preventing recurrences.

Prognosis, in general, depends upon the underlying myocardial condition. It is particularly poor whenever atrial flutter complicates myocardial infarction and when atrial flutter is an episode in terminal states. (Am.Heart J., February '51, G. R. Herrmann and M. R. Hejtmancik)

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Reconstruction of Defects of the Thoracic Wall with Tantalum Mesh Gauze: When tumors of the chest wall are radically removed or trauma leaves defects, herniation of the lung may occur unless some firm reconstruction is performed. The authors report a series of cases in which tantalum mesh gauze was used for repair of defects of the thoracic wall. They also review briefly various methods for accomplishing repair which have been used in the past.

Winkel, in 1935, wove strips of fascia lata between the ribs or endothoracic fascia to close a weakness in the thoracic wall. Watson and James modified this technic by closing the defects with single, large, free fascia lata grafts. Maurer and Blades, in 1946, used periosteal flaps and ribs cleaned of periosteum, cut across, and swung obliquely down to cover defects. They reported that Paulson had attempted to use a tantalum plate to cover a hernia of the lung, but had abandoned it because of the difficulty of immobilization. Beardsly used tantalum plate in 3 cases when reconstructing the chest wall after resecting large areas. The patients were comfortable, but in the 3 cases they developed serous drainage from around the plates, and in 2 cases, the serum became purulent. The plates were later removed in all 3 cases, after there had been a fibrous reaction around them giving stability to the thoracic walls. Campbell reconstructed the entire thickness of the anterior thoracic wall by freeing the latissimus dorsi muscle from its insertion and swinging it up into the defect, and covering the muscle with a free split thickness skin graft. When the skin is involved in the tumor, and has to be sacrificed, this method has advantages over the others that have been described. The surface can be epithelialized by a free graft, and dependence is not placed on flaps of skin and subcutaneous tissue, whose survival may be precarious.

When the skin and subcutaneous tissue do not have to be removed, the authors have used tantalum mesh gauze in reconstructing the thoracic wall. Tantalum mesh gauze is more pliable than plate, and has been used successfully in the repair of a variety of hernias: ventral, indirect inguinal, direct inguinal, obturator and recurrent inguinal. More conservative treatment, consisting of a corset with a pad or obturator over the deep defect can be used, but it is not curative. One prefers not to bury a foreign substance when repairing a thoracic hernia, but if the defect is large this method may offer a satisfactory solution.

In the 2 cases presented, tantalum mesh gauze (50 by 50 mesh of .003 inch tantalum wire) was used to reconstruct large thoracic defects. The tantalum mesh gauze has been well tolerated by the tissues during the relatively short period of observation. It is believed to be superior to tantalum plate when the defect occurs in the region of the ribs, where there is motion and shearing stresses and strains. The mesh can be fashioned to fit any type of defect, and is readily fixed in position with tantalum wire to bone or soft tissue. The plate would probably be more useful for repairing defects of the sternum, or for stabilizing the upper anterior thorax after removal of the manubrium and sternal ends of the clavicles. The gauze has remained in situ, and the patients have been fairly comfortable since the time of discharge.

The tumor in the first case was to all appearances a solitary plasma cell myeloma. In such cases, destruction or removal of this type of tumor appears justified. In the second case, the tumor was an adenocarcinoma of as yet undetermined origin. Operation has afforded the patient relief from pain, but there is some tenderness in the region of the repair, possibly due to irritation from the broken wires. (J. Thoracic Surg., February '51, A. E. W. Ada and E. P. Hevenor)

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The Feeding of Premature Infants: Because it had been noted that premature infants gained rapidly and did well when given a caloric intake considerably greater than that generally considered desirable, a study was undertaken on 3 groups of patients. Groups A and B consisted of infants, Negro and white, cared for in the premature nursery unit of the Harriet Lane Home, Johns Hopkins Hospital. In general, these infants came from families of very poor socioeconomic status; the majority were born either at home or in other hospitals and were transferred to the premature unit during the first 48 hours of life. Group C consisted of white infants, of considerably higher socioeconomic status, who were born and cared for in Sinai Hospital.

The infants in Groups A and B include only well premature infants who were cared for by essentially the same technics, and were given a formula consisting of partially skimmed milk with 10 percent dextrimaltose added to give a value of approximately 1 calorie per cc. (0.98 calorie per cc.). All feeding by

mouth was withheld for 24 to 48 hours, and in the very small infants occasionally for as long as 5 days; then 5 percent glucose solution was offered in small quantities for 12 to 24 hours before milk feedings were started. (Parenteral fluids were given when necessary to meet body fluid and electrolyte requirements.) The milk formula was then offered in small, gradually increasing amounts, allowing an increase of approximately 10 calories per kilo of body weight per day until an intake of 120 to 130 calories per kilo of body weight per day was reached at 10 to 14 days of age. The method of feeding, whether by gavage, medicine dropper, or nipple, was determined by the condition of the infant and its ability to suck and swallow. Supplementary vitamins A, C, and D were started on the 5th to 7th day of life. When the infant's weight reached approximately 2,200 Gm., the formula was changed, in preparation for discharge from the hospital, to a mixture consisting of equal parts of evaporated milk and water, with 5 percent carbohydrate added, giving a value of 0.86 calorie per cc. of formula. The feedings of the 47 infants in Group A were adjusted every 2 to 3 days so that an average intake of 120 to 130 calories per kilo of body weight per day was maintained.

The 51 infants in Group B were treated in the same manner as the infants in Group A, excepting that after 2 weeks of age the amount of formula offered was increased in accordance with the desires of the infant. No formula was forced upon an infant, but if the infant appeared hungry and willing to take more, the amount was gradually increased. In this group the infant taking the smallest amount averaged 121 calories per kilo of body weight per day while the one taking the largest amount averaged 195 calories per kilo of body weight per day.

The 47 infants in Group C were born and cared for at Sinai Hospital where the routines used in the nursery differed only slightly from those used in the Harriet Lane Nursery. The Sinai infants were fed a formula of half skimmed milk with 7 1/2 percent dextrimaltose added, with a caloric value of 0.85 calories per cc. Feedings were started 24 to 48 hours after birth and cautiously increased by 2 cc. increments to the point of tolerance.

Observations of caloric intake per kilo of body weight, number and character of stools, regurgitation or vomiting were recorded on each infant's chart every day. The infants were weighed 3 times weekly. The caloric intake for each infant from the time he reached 2 weeks of age until he reached 2,500 Gm. in weight or was discharged from the hospital was averaged. The infants in each group, A, B, and C, were separated, for the purposes of comparison, on a basis of birth weight, into three groups: those weighing 1,000 Gm. or less; those of 1,001 to 1,500 Gm., and those weighing 1,501 to 2,000 Gm.

Six of the 47 infants in Group A were discharged from the hospital weighing between 2,400 and 2,500 Gm.; 2 were discharged weighing between 2,000 and 2,100 Gm. Five of the 51 infants in Group B were discharged weighing between 2,070 and 2,380 Gm. Seven of the 48 infants in Group C were discharged weighing

between 2,225 and 2,395 Gm. The number of days necessary to reach 2,500 Gm. was estimated on the basis of previous weight gain for each infant and added to the number of days spent in the hospital.

In each weight group there was a very significant rise in the average daily weight gain as the caloric intake was increased and there was a corresponding decrease in the number of days of hospitalization necessary to reach a satisfactory weight for discharge. There was a greater difference between the results obtained in the 2 groups of babies (A and B) cared for in Harriet Lane than there was between the Group B babies with a relatively high caloric intake and those cared for at Sinai (Group C), who had an even higher caloric intake. The babies at Sinai at 2 weeks of age had not only regained their birth weight, but on the average surpassed this by a significant amount, thus helping to reduce the total days of hospitalization. This can be explained by the fact that these babies received a higher caloric intake during the first 2 weeks of life than did those at the Harriet Lane Home. The babies at Sinai averaged 3.9 and 4.1 stools per day as compared with 2.2 and 2.1 for the babies in Harriet Lane Home, suggesting that a larger amount of the calories given was not utilized than was the case in Harriet Lane infants.

Although the results of this experiment do not prove that high caloric diets are necessarily the optimum diets for premature infants, it is demonstrated that high caloric feedings will increase the average daily weight gain and will reduce the infant's hospital stay significantly. Furthermore, if the formula is increased cautiously and in accordance with the infant's desire, no ill effects are observed. (J. Pediat., February '51, J. B. Hardy and E. O. Goldstein)

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Aviation Medicine News: On Tuesday, 6 March, RADM Luis De Florez, USNR, gave a talk before the faculty and student flight surgeons of the School of Aviation Medicine, Pensacola, Florida. RADM De Florez, who was responsible for the organization of what is now known as the Special Devices Center, centered his discussion around aircraft instrumentation and human capabilities. A veteran of 39 years of flying (15 hours recently in a Jet), RADM De Florez described his early flights as being done in an aircraft with a top speed of 42 m.p.h., a cruising speed of 41 m.p.h., and a stalling speed of 40 m.p.h. He also commented on the advantages of Jet aircraft and the problem of pilot fatigue. (Av Med Schol, Pensacola, Fla.)

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NOW HEAR THIS: It is requested that when changing their address, personnel inform this office, giving full name, rank, corps, and old and new address.

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## Selected Research Reports

The Reaction Between Actomyosin and Various Nucleotides and Phosphates, as Followed by Ultraviolet Absorption: Interaction of actomyosin with adenine derivatives and phosphates was followed by ultraviolet absorption. Irreversible spectral changes were observed with ATP, ADP, A-5-MP and adenosine, but not with A-3-MP, adenine, phosphate buffer or sodium tripolyphosphate. These changes, characterized by an increase in optical density at wave lengths below 250 mμ and decrease above 250 mμ, caused a shift of the maximum absorption from 260 mμ to 250 mμ. On subtracting the actomyosin absorption from the observed optical densities at equilibrium, the spectrum obtained was that of hypoxanthine derivatives. The reaction was thus shown to be deamination of the adenosine derivatives.

In the actomyosin-ATP reaction with $Ca^{++}$ present, an early, reversible, spectral shift was superimposed upon the irreversible changes. The time course of this process closely paralleled that in viscosimetric studies of actomyosin. The optical density shifts were in different directions at different wave lengths. This suggests the process is due to changes in the actomyosin absorption rather than in amount of light scattered.

Dephosphorylation of ADP, ATP and sodium tripolyphosphate by 3-times and 4-times precipitated actomyosin was followed for four hours. For deamination under conditions resembling the experimental, the $\Delta F$ was estimated to be $-5000$ cal $mol^{-1}$; $\Delta F^{o}$ is about $-9200$ cal $mol^{-1}$. (Project NM 000 018.04.02, NMRI, NNMC, Bethesda, Md.)

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The Behavior of Free-Weighted Actomyosin Threads Under Pressure: Length was measured as a function of time and pressure, for free-weighted actomyosin threads immersed in a .001 M phosphate buffer solution. From these measurements upper limits were calculated for the numerical value of the pressure-volume term, $p(\partial V/\partial L)_{T,p}$, in the thermodynamic equation for the tension. It was found that this term was negligible compared to other terms of the equation and therefore that the ordinary method of obtaining the internal energy contribution to the tension is valid. At pressures above some 1000 lb. in $^{-2}$, the free-weighted threads lengthen irreversibly, and the lengthening stops when the pressure is removed. This is interpreted as another manifestation of the Marsland-Brown (viscosity) effect, and as being probably due to reduction in cross-linking of the gel. (Project NM 000 018.04.04, NMRI, NNMC, Bethesda, Md.)

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## From the Note Book

1. A complete Navy epidemic control laboratory, installed aboard a landing ship, LSI(L) for mobility and equipped to cope with epidemics of contagious disease, has arrived in the Far East. The new laboratory has been designated "Fleet Epidemic Control Unit One" and is manned by 2 MC officers, entomological, bacteriological and sanitation specialists, and 15 HC's, all hand-picked technicians. The success of this unit will be closely observed with a view toward organizing other units. (BuMed PIO, 5 March '51)

2. It is announced that the Civil Defense Administration will organize a national staff college to train state officials in civil defense technics. The course is scheduled to start 1 April 1951. Before summer, 3 area technical training schools should be under way. (Washington News, J.A.M.A., 24 February '51)

3. The Advisory Committee and panel chairmen of the BioSciences Group, Office of Naval Research, met in Washington on 19-20 February 1951 to discuss the role of the group in wartime research and emergency planning. The electronics program, manpower, London nutritional conference, Arctic research program, blood substitutes program, and burn research program were presented. (Bio Sciences Group, ONR, February '51)

4. It is reported that an amino acid mixture derived from lactalbumin, from which the more readily water-insoluble amino acids, such as methionine are removed, incorporated in a saturated fatty acid di-ester of polyethylene glycol base (Carbowax) applied to the affected area of pruritis ani gives immediate relief and, within a week, alleviation of pruritis symptoms. (Am.J. Dig. Dis., February '51, L. G. Bodkin and E. A. Ferguson)

5. New flexible vein strippers and the technics of vein stripping are described in Surgery, January 1951 by E. G. Emerson and J. J. Muller and in Surgery, February 1951 by C. M. Kutz and W. C. Hendricks, and by A. Webb, Jr.

6. "The Present Management of Varicose Veins" is discussed in the New England Journal of Medicine, 1 March 1951, by D. W. Barrow.

7. A sensitive colorimetric method for the determination of dicumarol in plasma is described in the Journal of Laboratory and Clinical Medicine, February 1951, by S. Roseman and H. Green.

8. More than 16 percent of the Regular Navy Medical Officers currently on duty hold certification by American Boards. In addition, 44 others have completed a portion of their Board Examinations. (Bu Med PIO, February '51)

9. An excellent symposium on "The Dynamics of Industrial Medicine" is presented by the several authors in the A.M.A. Archives of Industrial Medicine and Occupational Medicine, February 1951.

10. A symposium on the "Treatment of Amebiasis" by several authors appears in Postgraduate Medicine, February 1951.

11. Cdr. C. A. Boland, DC, USN, whose hobby is composing music, has been informed that he has been selected to receive an Honor Medal Award for 1950 from the Freedom Foundation for the prizewinning song entitled "I Like It Here." (BuMed PIO, February '51)

12. "What the Hospital Can Do About Disaster Planning" is discussed in Hospitals, February 1951, A. A. Rivin.

13. "Clinical Experience with Streptokinase and Streptodornase" is presented in J. A. M. A., 3 March 1951, J. M. Miller et al. (Refer to Medical News Letter, volume 17, no. 2, 26 January '51.)

14. An unusual study of warm clothing appears in Scientific American, March 1951, M. E. Barker.

15. "Observations on the Problem of Brucella Blood Cultures" is presented in the Journal of Bacteriology, February 1951, M. J. Pickett and E. L. Nelson.

16. "A New Surgical Treatment of Inguinal Hernia" appears in Journal of the International College of Surgeons, January 1951, A. Heffez.

17. "Tonsillectomy and Adenoidectomy and Poliomyelitis" is discussed in A.M.A. Archives of Otolaryngology, February 1951, A. H. Miller.

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Chlorination of Water Aboard Ship: It has been reported by a medical officer in the Pacific Fleet that there is some lack of information on the part of medical and engineering officers with regard to chlorination of ships' water supplies, that local regulations are not uniform, and that ships anticipating service in Asiatic waters should stock ample supplies of chlorinating agents.

Safeguarding the water on shipboard is a matter of importance at all times. When military operations are in progress, water-borne disease could have disastrous effect upon the efficiency of a ship. The Manual of Naval Hygiene and Sanitation NavMed P-126 (Revised 1949) devotes an entire chapter to water supply aboard ship in Paragraphs 40 through 46. On pages 173 to 176, the amcunt of chemical required is discussed. The Bureau of Ships Manual in Chapter 58,

Paragraphs 58-27 and 58-42 states that the bacteriological purity of distilled sea water may be subject to question if the salinity is in excess of 0.25 grains of sea-salt per gallon and sets forth instructions for operation of ships' distilling plants in potentially contaminated waters.

Pacific Fleet Regulations require bacteriological examination of water intended for human use and chlorination when necessary. Fleet and Force letters and directives promulgate information concerning chlorination procedures. These instructions may vary slightly, but should be in substantial agreement with the information provided in the Manual of Naval Hygiene and Sanitation which should be readily available on all ships.

The medical officer should be alert to prevent danger of water-borne disease. When there is doubt concerning the safety of the water supply, it should be chlorinated. The initial dose of chlorine may be calculated from Table I, and additional chlorine added as necessary to maintain a residual of at least 0.1 ppm free chlorine as directed by the Manual of Naval Hygiene and Sanitation and fleet regulations. It will be noted that while 1 ounce of 70 percent available chlorine per 5,000 gallons will provide an ample level in chemically fairly pure water, as much as 1 ounce per 1,000 gallons of water may be required to satisfy chlorine demand and establish a residual in waters containing much organic matter. Thus, the daily requirement for a medium sized ship could be as great as 2 pounds in unusual circumstances.

TABLE I

| Tank Capacity in Gallons | Stock Number and Amount of Chlorinating Agent in Ounces to Provide 1 ppm | | |
|---|---|---|---|
| | Calcium Hypochlorite 70% available chlorine 51-C-452 | Chlorinated Lime 35% available chlorine 51-L-326 | Sodium Hypochlorite Solution 10% available chlorine 51-S-3299 |
| 500 | 0.1 ounce | 0.2 ounce | 0.7 fl. ounce |
| 1,000 | 0.2 " | 0.4 " | 1.3 " " |
| 1,500 | 0.3 " | 0.6 " | 2.0 " " |
| 2,000 | 0.4 " | 0.8 " | 2.6 " " |
| 3,000 | 0.6 " | [illegible] " | 3.9 " " |
| 4,000 | 0.8 " | 1.6 " | 5.2 " " |
| 5,000 | 1.0 " | 2 " | 6.4 " " |
| 10,000 | 2 " | 4 " | 13 " " |
| 15,000 | 3 " | 6 " | 19 " " |
| 20,000 | 4 " | 8 " | 26 " " |
| 25,000 | 5 " | 10 " | 32 " " |
| 50,000 | 10 " | 19 " | 64 " " |

For individual canteen water purification, Water Purification Tablets, stock number 51-T-4278,should be stocked. These tablets are provided in bottles of 50 for iodine purification of small amounts of water, as in the case of canteens for landing parties. (Preventive Med. Div., BuMed)

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List of Recent Reports Issued by Naval Medical Research Activities:

Naval Medical Research Institute, NNMC, Bethesda, Maryland.

Some Studies on the Infrared Absorption of the Contractile System of Skeletal Muscle, NM 000 018.04.03, 23 June 1950.

A Recording Two-Channel Photofluorometer for In Vivo Studies with Fluorescein, NM 007 081.07.06, 23 August 1950.

Experimental Infections with Plasmodium fallax Schwetz Isolated from the Uganda Tufted Guinea Fowl, Numida meleagris major Hartlaub, NM 005 048.01.02, 27 November 1950.

Filariasis in American Samoa. I. Loss of Microfilaria in the Absence of Continued Reinfection, NM 005 048.08.01, 1 December 1950.

Performance Characteristics of BuShips Footwarming Panel Designed for Use in Semi-Exposed Bridge Areas of Ships, Proj. X-189, Report No. 12, 21 December 1950.

Decrease of Adrenal Ascorbic Acid and Cholesterol in the Rat and Guinea Pig, Following Large Doses of Glutathione, NM 007 081.11.01, 27 December 1950.

U. S. Naval School of Aviation Medicine, USNAS, Pensacola, Florida.

Composition of Alveolar Air and Volume of Pulmonary Ventilation During Long Exposure to High Altitude, NM 001 059.03.08, 15 December 1950.

Alignment of Histological Radioautographs by Means of a Shadow Replica of the Tissue Pattern, NM 001 059.23.01, 9 January 1951.

U. S. Naval School of Aviation Medicine, USNAS, Pensacola, Florida, and Tulane University.

Studies in Space Perception, NM 001 063.01.18 (formerly NM 001 37), 31 October 1950.

Age as a Variable in Post Rotational Phenomena, NM 001 063.01.19, 1 November 1950.

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Third Annual Navy Industrial Health Conference: As previously announced in the Medical News Letter, volume 17, number 4, page 19 (23 February 1951), the third annual Navy Industrial Health Conference will be held in Atlantic City, at the Chalfonte-Haddon Hall. Information then given included a list of Atlantic City hotels.

BuShips, BuAer, BuSandA and BuOrd have advised that announcements regarding the conference, with copies of the preliminary program as enclosures, will be issued to field establishments under their representative management controls. Because of this active support of the conference by these Bureaus, it is predicted that attendence this year may exceed original expectations. BuMed may find it necessary to make arrangements for a larger hall than the one already engaged. Senior Medical Officers are requested, therefore, to submit a list of personnel who will attend the conference to the Bureau of Medicine and Surgery, Att: Industrial Health Section, at the earliest possible date.

Three of the 5 meetings of this year's conference have been arranged in the form of panel discussion, with careful attention being given in selecting topics for discussion and panel members who will be representative of every type of naval field establishment. Delegates to the conference will be requested to submit written questions prior to the meetings. The moderators of panels will choose those questions for discussion which appear to be most helpful and informative to the group as a whole. It is probable that in drawing up this preliminary program omission may have been made of the names of medical officers whose presentations to the group would be highly desirable. In submitting the names of conference delegates, suggestions for individuals or topics that should be included on the program and questions desired for discussion may be included in the letter.

Occupational medicine and industrial hygiene must keep pace with the introduction of new processes and new materials, with new concepts of job placement through physical evaluations, with new technics for detection of occupational disease in its incipient stage, with new measures for promotion and maintenance of optimum worker health, and with trends in occupational disease compensation laws. These vitally important topics will be discussed at this Conference.

As soon as enough names of delegates have been received to indicate whether the original preliminary program needs any modification, a final program will be issued to all Medical Departments which have expressed intention of being represented at the meetings. Present indications are that this will be a most successful conference. Senior Medical Officers are urged to do everything possible to convince commanding officers of the advantage of representation. (Preventive Med. Div., BuMed)

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BUMED CIRCULAR LETTER 51-39 23 February 1951

From: Chief, Bureau of Medicine and Surgery
To: All Holders of the Bulletin of Bureau of Medicine and Surgery Circular Letters

Subj: Quarters, Heat, Light, Household Equipment, Subsistence and Laundry Furnished Certain Civil Employees of the Medical Department; Utilities and Maintenance Furnished Navy and Marine Corps Exchanges and Commissioned Officers' Messes (Open)

Ref: (a) BuMed Cir Ltr No. 44-99
(b) BuMed Cir Ltr No. 44-148
(c) BuMed Cir Ltr No. 45-140
(d) BuMed Cir Ltr No. 46-136
(e) BuMed Cir Ltr No. 48-135
(f) SecNav Ltr of 17 Oct 1949; NDB July - Dec 1949, 49-759, p.42
(g) BuDocks Ltr C-344A/sfm N26-5 of 8-11-50
(h) BuSandA Manual Volume 6, Chapter 6, part E
(i) Marine Corps Manual, par. 18054
(j) USN Exchange Regulations, par. 202

References (a) to (e) inclusive are hereby cancelled and superseded by the instructions contained in this letter.

This letter outlines the authority for and the procedures required in annual appraisals of the value of quarters, utilities and subsistence furnished to civilian employees, Red Cross uniformed personnel, and rates to be charged Navy Exchanges and Commissioned Officers' Messes (Open).

The letter will not be published in the Navy Department Bulletin.

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BUMED CIRCULAR LETTER 51-40 27 February 1951

From: Chief, Bureau of Medicine and Surgery
To: All Medical Department Activities and Facilities

Subj: Unofficial questionnaires; handling of

1. The Bureau's attention has been called to the fact that field Medical Department activities have been requested by commercial sources to complete questionnaires relative to their present inventories of and future requirements for surgical and hospital equipment.

2. It is directed that Medical Department activities receiving such requests return them with a courteous explanation that the information requested is restricted to official government use and is not otherwise available. They may also be advised that future requests for information pertaining to the Medical Department should be directed to the Chief, Bureau of Medicine and Surgery, Department of the Navy, Washington, D. C.

H. L. Pugh

The above letter will not be printed in the Navy Department Bulletin.

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BUMED CIRCULAR LETTER 51-41 27 February 1951

From: Chief, Bureau of Medicine and Surgery
To: All Ships and Stations

Subj: Policy regarding BuMed's recommendations on changes in rating from Group X (Medical) to Group XI (Dental) within the Hospital Corps

Ref: (a) BuMed Circular Letter 50-132

1. Reference (a) is hereby cancelled.

2. The Bureau will not recommend favorably to the Chief of Naval Personnel on the following:

(a) Requests from Group X personnel (male or female) for a course of instruction at a U. S. Naval Dental Technician School (Class A) with an ultimate change in rating to the Dental Rating Group.

(b) Requests for changes in rating from Group X to Group XI in the case of male personnel holding a certificate of instruction or who have been designated Dental Technician, General by the Bureau.

3. However, a change of rating will be recommended for:

(a) Male or female personnel designated Dental Technician, Prosthetic.

(b) Female personnel designated Dental Technician, General, or who, by virtue of civilian education and/or occupation are qualified Dental Assistants or Dental Hygienists.

4. All requests for changes in rating must be accompanied by substantiating affidavits, the recommendation of a dental officer, and a Report of Examination for

a Change in Rating (NavPers-624). The requests must be forwarded to the Chief of Naval Personnel via this Bureau and other official channels.

H. L. Pugh

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BUMED CIRCULAR LETTER 51-42 28 February 1951

From: Chief, Bureau of Medicine and Surgery
To: All Ships and Stations

Subj: Sulfanilamide powder in first aid dressing kits; discontinuance of use of

1. Sulfanilamide powder for local application to wounds is no longer recommended for use nor catalogued by the Bureau of Medicine and Surgery. However, certain units of Armed Services Catalog of Medical Materiel stock number 2-017-455, "Dressing, First Aid, Individual Troop, Camouflaged, Small," procured under a specification now cancelled, consist of a 5 gram packet of sulfanilamide powder and a battle dressing in a sealed container. Since accidental use of this sulfanilamide powder in isolated instances would not be hazardous enough to justify destruction of the stock of kits on hand, the units with sulfanilamide powder will continue to be issued until the stock is exhausted.

2. Accordingly, medical officers are directed to instruct personnel to discard sulfanilamide powder found in individual troop first aid dressings at the time each such kit is opened for use.

H. L. Pugh

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BUMED CIRCULAR LETTER 51-43 1 March 1951

From: Chief, Bureau of Medicine and Surgery
To: All Ships and Stations having Dental Personnel

Subj: Assignment of Navy Job Classification to Group XI (Dental) Personnel

Ref: (a) Manual of Enlisted Navy Job Classifications (NavPers-15105, Rev.)

1. In order to more effectively utilize the Navy Job Classification system and to ensure that Group XI (Dental) personnel are assigned a classification which will most adequately reflect their level of skill, it is the desire of this Bureau that the following policy be applied, effective immediately.

(a) All personnel completing a course of instruction at U.S. Naval Dental Technician Schools (Class "A" or "C") will be assigned the appropriate basic Navy Job Classification.

(b) As a person develops a higher level of skill in this particular occupational field he may be advanced in classification, however, extreme care should be exercised to ensure that only the most fully qualified personnel are assigned a supervisor's job code.

(c) Under no circumstances shall a person's job classification be changed to another occupational field (i.e., from Dental Technician, General 8700-8709 to Administrative and Clerical 8720-8729) within the Dental Group, without the prior approval of this Bureau.

2. Report all changes in Navy Job Classification immediately to this Bureau on NavMed HC-3 card.

H. L. Pugh

The above letter will not be printed in the Navy Department Bulletin.

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BUMED CIRCULAR LETTER 51-44 5 March 1951

From: Chief, Bureau of Medicine and Surgery
To: CO, All Naval Hospitals, Continental United States

Subj: Film strip - Certification of Causes of Death

1. The method of reporting causes of death recommended by the World Health Organization was adopted by the Navy in 1949, and has now been adopted also by the various states. Death certificates required by civilian agencies in the United States will provide for stating the cause of death in essentially the same way as shown in section 27 of NavMed-N, Certificate of Death (revised 1-1-49).

2. The U. S. Public Health Service has prepared a film strip and record explaining the correct method of reporting cause of death on the new forms, and has provided each state health department with copies for distribution on a loan basis within the state.

3. It is recommended that continental naval hospitals take advantage of the opportunity to show the film strip to their staff medical officers. It is particularly helpful in connection with death certificates required by civilian agencies; however, almost all of the film strip applies equally well to the cause of death section of NavMed-N. It should therefore clarify the method of reporting cause of death on both civilian and Navy death certificates.

H. L. Pugh

BuMed Circular Letter 51-44 will not be printed in the Navy Department Bulletin.

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BUMED CIRCULAR LETTER 51-45 7 March 1951

From: Chief, Bureau of Medicine and Surgery
To: Holders of Bulletin of BuMed Circular Letters

Subj: Correspondence Training Division, U. S. Naval Medical School; establishment of

1. A Correspondence Training Division will be established at the U. S. Naval Medical School, National Naval Medical Center, Bethesda, Maryland, on 15 March 1951. This division will plan, produce, and administer Medical Department correspondence training courses for medical personnel of the Regular and Reserve components of the Navy.

2. All reserve correspondence course functions and responsibilities, except for dental personnel, heretofore conducted in the Bureau of Medicine and Surgery, have been assigned to the Correspondence Training Division, U. S. Naval Medical School.

3. The purpose of the correspondence training courses is to afford Medical Department personnel the means of acquiring detailed knowledge of those professional and technical subjects peculiar to the Naval Service. These courses also provide retirement credits under the provisions of Public Law 810, 80th Congress.

4. On and after 15 March 1951, personnel of the Medical, Medical Service, Nurse, and Hospital Corps of the Regular and Reserve components should submit their requests for enrollment in the Medical Department correspondence courses to the Commanding Officer, U. S. Naval Medical School, National Naval Medical Center, Bethesda 14, Maryland.

5. The Medical Department correspondence courses for the personnel of the Dental Corps and dental ratings will continue to be administered in the Bureau of Medicine and Surgery. These personnel should submit their requests for enrollment in the courses to the Bureau of Medicine and Surgery, Attention: Chief, Dental Division.

H. L. Pugh

The above letter will not be printed in the Navy Department Bulletin.

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